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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/187,661	11/06/1998	BRET A. SHIRLEY	5784-3	3329

27476 7590 09/08/2004

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Intellectual Property - R440
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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/187,661	SHIRLEY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,13,16-20 and 28-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 13, 16-20 and 28-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed June 21, 2004 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 1, 3, 4, 13, 16-20 and 28-50 are pending.

Applicants' amendment filed June 21, 2004 is acknowledged, and applicants' response has been fully considered. Claims 19, 39, 41 and 44 have been amended. Therefore, claims 1, 3, 4, 13, 16-20 and 28-50 are examined.

Objection Withdrawn

3. The previous objection of claims 19, 39, 41 and 44, is withdrawn in view of applicants' amendment of the claim, and applicants' response at page 6 in the amendment filed June 21, 2004.

Rejection Withdrawn

Claim Rejections-Obviousness Type Double Patenting

4. The previous rejection of claims 4, 13, 19, 20, 33, 37, 39-44, 49 and 50 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-48 and 85-112 of copending Application No. 09/188,051, is withdrawn in view of applicants' response at pages 6-7 in the amendment filed June 21, 2004.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 3, 16-18, 28-32, 34-36, 38 and 45-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-48 of U. S. Patent 6,767,892 (the previous copending application 09/188,051). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3, 16-18, 28-32, 34-36, 38 and 45-48 in the instant application disclose a low salt-containing aqueous composition comprising biologically active human IGF-I or a functional variant thereof in a concentration of about 250 mg/ml and a pH about 5.0 or greater, wherein the variant has at least 80% sequence identity to human IGF-I. This is obvious in view of claims 1-48 of the patent which disclose a composition having a pH of 5.5 or greater, comprising IGF-I or a biologically active analog thereof having at least 70% sequence identity to human IGF-I at a concentration of about 12 mg/ml to about 200 mg/ml, and at a temperature of about 4 ^{o}C, and a solubilizing compound comprising a guanidinium group, wherein the solubilizing compound is in an amount sufficient to make IGF-I or analog thereof soluble. Since the term "about" is not defined in the specification of the instant application, and the specification indicates that "low salt" is intended an amount of salt that is in insufficient to cause precipitation of the protein (see page 4, lines 11-13), the highly concentrated and low-salt IGF-I syrup is prepared by adding solubilizing agent such as arginine, followed by removal of the solubilizing agent (page 4, line 30-page 5, line 5;

page 7, lines 5-23), and the IGF-I syrup is preferably stored at a temperature of about 2-10 °C, most preferably at 4 °C with a shelf life of 18-24 months (page 12, lines 6-9); and furthermore, the specification of the patent discloses the IGF-I composition may be formulated with a pharmaceutically acceptable excipient or carriers, or may be formulated in a sustained release or gel formulation (column 9, lines 23-59), IGF analogs have at least 70% sequence identity to reference IGF-I and may differ from the reference IGF-I by 5, 4, 3, 2 or 1 amino acids (column 4, lines 29-35), and IGF-I may be obtained from recombinant methods (column 7, lines 1-11), thus, the low salt-containing composition can be a composition containing a salt such as arginine in an amount that makes IGF-1 or its analog more soluble at higher concentration and at about 4 °C, and the concentration of IGF-1 is about 250 mg/ml (which can also be about 200 mg/ml). Both sets of claims encompass a low salt-containing (e.g., arginine) aqueous composition comprising human IGF-I or a biologically active variant thereof at a concentration of about 250 mg/ml and a pH about 5.0 or greater, wherein the variant has at least 80% sequence identity to human IGF-I. Thus, claims 1, 3, 16-18, 28-32, 34-36, 38 and 45-48 in present application and claims 1-48 in the patent are obvious variations of a low salt-containing aqueous composition comprising human IGF-I or a biologically active variant thereof at a concentration of about 250 mg/ml and a pH about 5.0 or greater, wherein the variant has at least 80% sequence identity to human IGF-I .

In response, applicants indicate the present application teaches a highly concentrated IGF-I formulation (see page 4 of the present specification), whereas the teachings in the '051 application are directed to compositions in which IGF-I is highly soluble at pHs of about 5.5 or greater and at refrigerated temperatures (see page 3 of the '051 specification); a claim chart,

which is included to highlight these differences, shows specific claim limitations present in the independent claims, claims 1, 34 and 42 of the present application, as compared to the corresponding independent claims of the '051 application. As can be seen, the concentrations of IGF-I recited in all of the independent claims of the '051 application are limited to 12-200 mg/ml, whereas the corresponding concentration in the present application is 250 mg/ml or greater in claims 1 and 34, and 350 mg/ml in claim 42. Thus, a composition including an IGF-I concentration of 250 mg/ml in a highly concentrated form is certainly patentably distinct from a composition including IGF-I at a concentration of at most 200 mg/ml in a highly soluble form; each independent claim of the '051 application has a temperature limitation of 4 degrees Celsius, a limitation not found in the independent claims of the present application; each independent claim of the '051 application requires a solubilizing compound, a limitation not found in the corresponding independent claims of the present application; and claim 42 of the present application contains two additional limitations (density and viscosity) not found in the independent claims of the '051 application. These limitations would not be obvious in light of the claims of the '051 application. Therefore, the formulations of the present application and the '051 application differ in structure and function (pages 6-7 of the response).

Applicants' response has been considered, however, the argument is not found fully persuasive because of the following reasons:

The concentration in the present application is about 250 mg/ml or greater in claims 1 and 34, and about 350 mg/ml in claim 42, while the concentrations of IGF-I in the independent claims of the '051 application are limited to about 12 to about 200 mg/ml. Since the specification does not specifically define the term "about", the concentration of about 250 mg/ml

can be 200 mg/ml. Furthermore, the specification of the instant application discloses the term "low salt" is intended an amount of salt that is in insufficient to cause precipitation of the protein (see page 4, lines 11-13), the highly concentrated and low-salt IGF-I syrup is prepared by adding solubilizing agent such as arginine, followed by removal of the solubilizing agent (page 4, line 30-page 5, line 5; page 7, lines 5-23), and the IGF-I syrup is preferably stored at a temperature of about 2-10 °C, most preferably at 4 °C with a shelf life of 18-24 months (page 12, lines 6-9), thus, even the limitations such as "at a temperature of about 4 °C" and " a solubilizing compound comprising a guanidinium group" are not cited in the claims, it is obvious that these limitations are encompassed by the claims from the teachings of the specification of the instant application. Therefore, a low salt-containing aqueous composition comprising an IGF-I concentration of about 250 mg/ml is not patentably distinct from a composition comprising IGF-I at a concentration of about 200 mg/ml in the presence of a solubilizing agent. Regarding the composition of IGF-I in a concentration of 350 mg/ml having a density of about 1.07 g/ml and a viscosity of about 15,700 cps, applicant's argument is persuasive, thus the rejection of claims 4, 13, 19, 20, 33, 37, 39-44, 49 and 50 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 3, 4, 13, 16-20 and 28-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 4, 13, 16-20 and 28-50 are indefinite because of the use of the term "A low salt-containing aqueous composition". The term cited renders the claim indefinite, it is not clear what concentration of salt in the composition is as to "A low salt-containing aqueous composition". The specification indicates "low salt-containing" is intended an amount of salt that is in insufficient to cause precipitation of the protein (page 4, lines 11-13), while the conditions of the solution such as buffer, the identity of the salt and the concentration of the protein are not indicated, it is not clear what is the concentration of low salt that does not cause precipitation of the protein, e.g., is it 10, 20, 50 or 100 mM, or 1 M? Claims 3, 4, 13, 16-20, 28-33, 35-41 and 43-50 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
August 31, 2004